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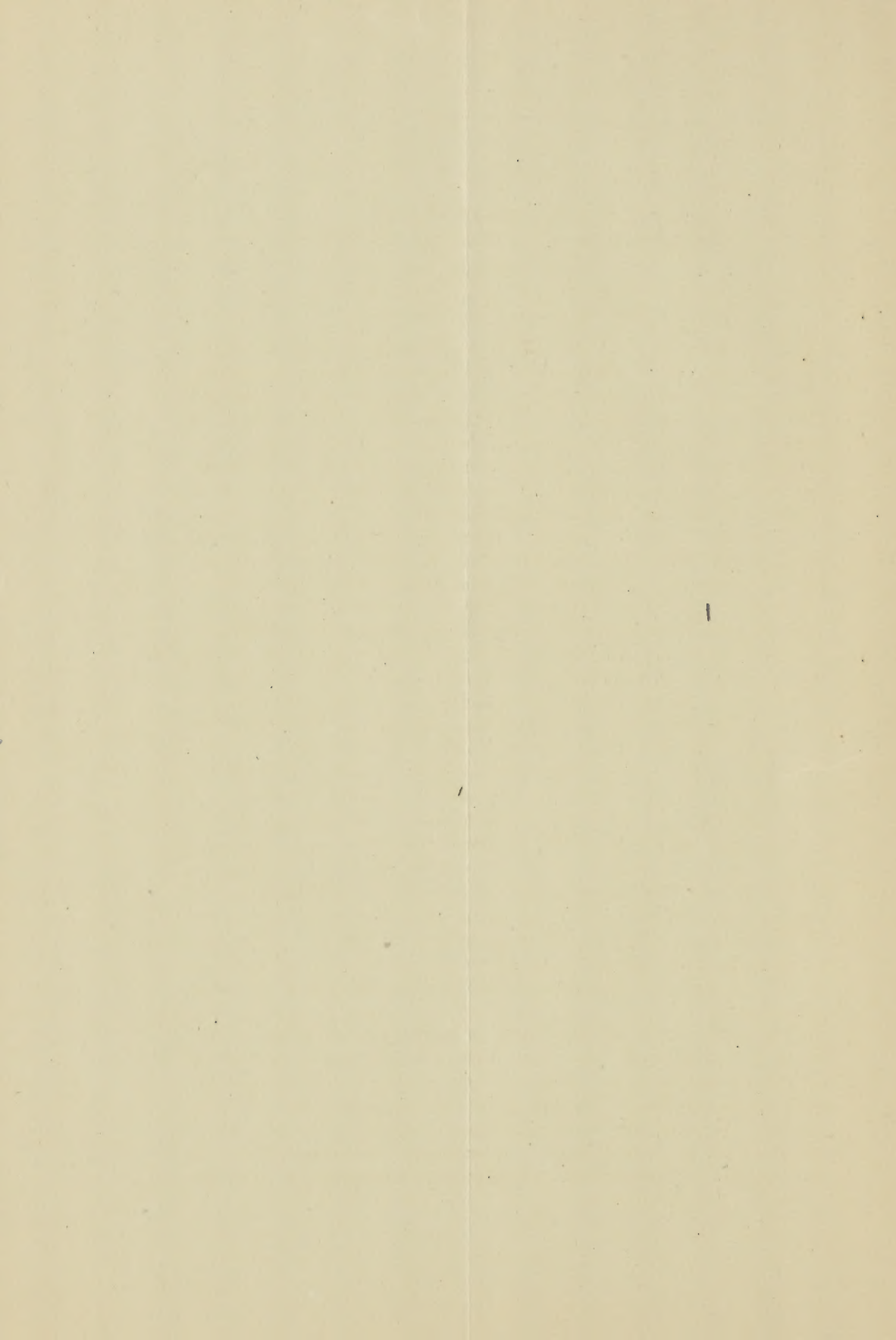
A SECOND CASE.

BY

JAMES C. WHITE, M. D.,
Professor of Dermatology in Harvard University.

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IN the JOURNAL OF CUTANEOUS AND GENITO-URINARY DISEASES for June, 1889, I published the account of a remarkable case of cutaneous disease, such as I had never seen before, and of which I could find no description in literature. It was characterized by concretions of epithelial cells, varying in size from the head of a pin to horn-like masses of half an inch in height, which had their origin within the mouth of the sebaceous glands, and occupied nearly the whole surface of the body. I called the disease, therefore, keratosis follicularis.

At the International Congress of Dermatology, held at Paris in August, a patient was shown as an example of an affection described by Darier, *chef du laboratoire de la Faculté à l'hôpital Saint-Louis*, in the "Annales de dermatologie et de syphiligraphie," July 25, 1889, under the title *psorospermo folliculaire végétante*. The same affection had formed the subject of a "Thèse de Paris" by Dr. A. Thibault, May 8, 1889. M. Darier had previously made a communication upon the subject before the Société de biologie on March 25, 1889. The observations of these gentlemen, unknown to me before the meeting of the congress, were based upon two cases of the affection which had been seen at the Saint Louis Hospital during the preceding year. One of these was the patient exhibited to the congress, and the appearances he presented were identical with those of my patient, although the lesions in the former were far less developed in diversity and magnitude, as the duration of the disease was only eight years. I had no hesitation in pronouncing the affection to be the same as that described by myself under the name keratosis follicularis, and stated further that, although I was not prepared to deny the correctness of M. Darier's conclusions as to the parasitic nature of the peculiar cells found in the epidermal concretions, neither Dr. Bowen, who had made the microscopic studies in my case, nor myself had recognized them as of such a character.

The conclusions of M. Darier may be briefly stated as follows: There exists in man a group of cutaneous diseases, which deserve the name of psorospermoses, due to the presence in the epidermis of parasites of the order of sporozoaires. This class includes the gregarinæ, the oval psorospermæ or coccidiæ, the sarcosporidiæ, the psorosperms of fishes or myxosporidiæ, and the psorosperms of the articulates or microsporidiæ. All these organisms live as parasites upon other animals, and give rise, in certain



cases, to fatal diseases. The coccidiæ, to which the forms in question are claimed to belong, inhabit almost exclusively the epithelial tissues of vertebrates. They are distinguished from the sporozoaires, especially the gregarinæ, by absence of movements at any period of their development, their intracellular habitat, their solitary encystment, and by the limited number of spores which develop in the cysts. Among the best known is the oviform coccidia of the biliary ducts of the rabbit, where it produces cysts. In the affection *psorospermose folliculaire végétante* coccidiæ of a

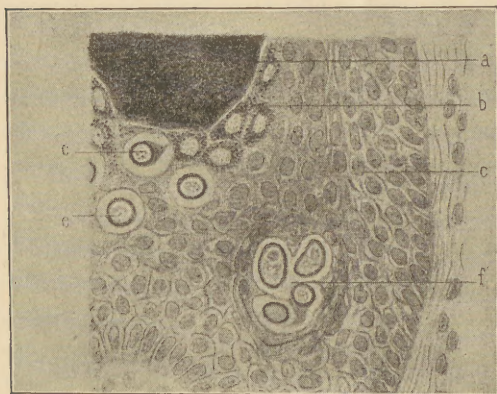


FIG. 1.—EPIDERMAL PLUG, NEIGHBORHOOD OF A HAIR FOLLICLE INVADDED BY PSOROSPERMS.

a, stratum corneum; b, stratum granulosum; c, stratum Malpighii; e, e, f, encysted psorosperms.

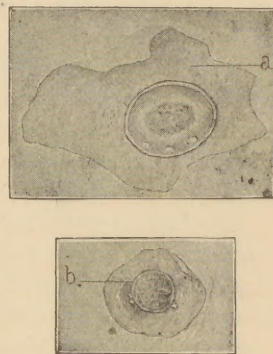


FIG. 2.—TWO CELLS FROM THE DEEPER PORTION OF A FOLLICULAR PLUG, EACH CONTAINING AN ENCYSTED COCCIDIA.

Reproduction, in part, of the illustrations of M. Darier's paper.

particular kind invade the follicular orifices under the form of round bodies, generally encysted and contained within the epithelial cells, or of refracting granules, the accumulation of which forms a plug, which projects from the mouths of the follicles. The presence of these parasites establishes the diagnosis of this disease, inasmuch as they are not met with in any clinically analogous affection. The neck of the follicles thus attacked becomes secondarily the seat of papillomatous affections, which may become enormously developed and be converted into real tumors. This affection, in its ætiological relations, should be placed with Paget's disease,* and probably with molluscum contagiosum.

* In a paper presented to the congress by Dr. Louis Wickham, *interne de l'hôpital Saint-Louis*, on "The Pathological Anatomy of Paget's Disease," he describes the microscopic appearances as follows: "In accordance with Darier, he was able to affirm that the peculiar cellular alterations of the epidermis and of its prolongations, formerly considered, in order to explain the difficulty away, either as consisting of degenerated cells, or as of cells in process of endogenous transformation, are no other than parasites belonging to the class of sporozoa, of the order of psorospermose. These parasites were seen in different stages of their evolution. At the commencement they consisted

Early after my return from the congress there presented herself at my clinic at the Massachusetts General Hospital a case sent by Dr. Everett, of Worcester, for diagnosis, under whose observation it had been for eighteen months. The forehead and posterior portions of the cheeks, as low as the angles of the jaw, were thickly occupied by discrete, dry, firm, brownish papular elevations, semi-globular in shape, and varying in size from a small to a large pin's head. The same lesions were more sparsely distributed on the sides of the nose and on the chin, where they had more recently appeared. They were also present on the neck and upper front chest. The backs of the hands presented also many minute, flattened, and smooth papules, which had the color of the normal skin. All these appearances might not, perhaps, have excited particular attention if seen before acquaintance with those of my first case, especially as the face at this visit was in a state of active inflammation, resulting from the action of applications then in use. An examination of the lower abdomen, hips, and upper thighs showed, however, the presence of much larger and more striking lesions, which confirmed the correctness of the suspicions aroused by the appearances upon the exposed parts of the skin. These surfaces presented numerous firm hemispherical and conical prominences, of a dark-brown color, two or three times as large as those above described, and more horn-like in consistence. They were all seated above the mouths of the sebaceous glands; over the pubes they were the most abundant and largest. They resembled in all particulars the lesions of the same grade of development in the case reported by me in the *JOURNAL OF CUTANEOUS AND GENITO-URINARY DISEASES* in June, and in that exhibited at the Paris Congress, above referred to. The disease was recognized by Dr. Bowen and myself as unmistakably identical with the former.

The patient was a girl twenty-one years old, and her history, as given by Dr. Everett and herself, was as follows: At the age of five or six there were dry and brown patches on the sides of her forehead, so that her playmates used to tell her that she had a dirty face. When she was fifteen this condition nearly covered her forehead. It appeared on her wrists, lower body, and thighs, also in early childhood; but she feels sure that it is less abundant upon the latter parts now than some years ago. The lesions upon the hands,

of amœboid masses, very difficult to distinguish from cellular protoplasm. The cell which contained the parasite increased considerably in size, and presented a more irregular form. At a given time the parasite became encysted, and its capsule, at first not clearly defined, became perfectly round, thickened, and brilliant. A distinct, enormously developed nucleus was then visible in the cell, having a round body and brilliant double contour, and in the central protoplasmic contents were to be seen two or several nuclear forms, which are no other than the pseudo-navicellæ. These distinct, well-developed bodies are coccidiæ, or psorospermia, in their adult condition. He believed that the presence of the parasites explained the pathological lesions."—From "Report of Congress," by Wickham, in "*British Journal of Dermatology*," October, 1889.

too, have become less distinct under the various treatments employed. The disease has extended upon the lower face within the last six months. The patient's left leg was amputated at mid-thigh, at the age of sixteen, for "white swelling" of the knee, which lasted nine years; and her general condition is not good.

After the examination of the patient had been completed the surprising discovery was made that the person described in my former article, whom she then accidentally met in the waiting-room, was her own father. This astonishing coincidence of so rare an affection in two members of one family naturally suggested the question of its possible bearings upon its aetiology, for, if we accept the views of M. Darier as to its parasitic nature, might not this concurrence be regarded as important evidence in favor of its communication from father to daughter by contagion? It was found on inquiry, however, that the daughter had been adopted by another family in infancy, and that her father had not seen her since she was a year old. This circumstance, although not absolutely excluding the possibility of the transference of the disease to her in this way, reduces the chance of such an occurrence to a minimum. There had been another child in the family, but it had died at the age of five, with a fair skin.

The question of heredity naturally suggests itself as furnishing a possible explanation of the appearance of the disease in Case II, an aetiological factor, as we know, of more potent influence in affections of the epidermal layers than in those of the other cutaneous structures.

Specimens of the concretions were removed from various parts by the cutaneous punch, and examined by Dr. Bowen. It may be briefly stated in advance that the structure of the lesions was shown to be identical with those of a corresponding degree of development in the first case, and that the modified epithelial masses contained the same peculiar cells or bodies as were found in the latter and in the French cases.

DEAR DR. WHITE: I have made a further examination, as you requested, of the lesions of Case I, in the light of M. Darier's researches, and have also studied those removed from Case II.

The lesions removed from the thigh in Case II showed the same appearances found in Case I—namely, a dilatation of the mouths of the follicles, this enlarged space being filled up with a horny mass. The same prolongation of the rete into the corium was also observed. In the lesions examined there was, too, no implication of the glandular structures. In a word, there can be no question of the anatomical identity of the lesions of the two cases.

Examination of some newly excised pieces from Case I demonstrates unequivocally the fact that Darier's cases represent the same pathological process as these two. The cells which he considers to be animal parasites belonging to the sporozoa are to be found in both Case I and Case II—namely, round bodies possessing a highly refractive membrane, usually containing a nucleus, and often appearing to be encysted. I find that their characteristics agree

in so many respects with the description of Darier that I shall confine myself to a few particulars in which I am unable to record the same results as this author.

1. Their intra-epithelial situation was not so clearly shown in my specimens. After softening the horny plug that filled the follicular orifice in a little dilute ammonia and staining with hæmatoxylin, the microscope gave the picture of numbers of round bodies with a highly refractive contour, usually less deeply stained than the more central portion, where a nucleus could often be observed, and, together with these, the ordinary epithelial cells and shreds. After looking over a large number of specimens with the greatest care, I could find but one or two places which suggested the appearances pictured by Darier in his Plate IV, Fig. 3, and Plate V, Fig. 7—namely, an epithelial cell containing the psorosperm-like body, with the appearance of a nucleus pushed to one side. In the few instances where I was able to find these appearances I could not definitely satisfy myself or others that the round bodies were not simply closely adherent to the underlying cell rather than contained in its protoplasm. Possibly the difference in results was due to an imperfect application of Darier's method, as he speaks of these appearances as very readily seen. Certainly their importance in considering the nature of these bodies can not be questioned.

2. Darier makes no mention of a process of cornification, but it seems very difficult to believe that there is not a hyperkeratosis taking place in these lesions, whether or not these bodies be coccidiæ. In the first place, the stratum granulosum in the dilated follicular mouths is greatly increased in width and in many places in the size of the granules, as is constantly shown in sections stained with hæmatoxylin and afterward treated with a one-per-cent. solution of hydrochloric acid. Moreover, it can be readily seen, in sections so treated, that the round, psorosperm-like bodies at the level of the stratum granulosum are affected in the same way by the reagents as the neighboring tissue cells, for they contain the deeply stained granules of eleidine. Above this layer these bodies are found to be scarcely or not at all stained, like the cells of the stratum corneum about them, and their outlines can be made out only in the lower portion of this layer. In Case I the horny plugs projected from the follicles to the extent of half an inch in some places, and the outer portion of the plug had precisely the appearance and consistency of a firm horn. Microscopically, sections cut parallel with the long axis of the horny plug showed the round, psorosperm-like cells at the base of the concretion, and they could be traced upward for some distance, gradually becoming flattened and fused together, until in the firm, hard, upper portion the mass is composed almost entirely of lamellæ, having much the appearance of broad bands of fibrous tissue, arranged in bundles running vertically and obliquely, and containing small elongated nuclei. Between these fibrous-like bands picocarmine staining differentiates in some places aggregations of round, loosely connected, highly refractive cells; but the lamellæ make up the greater part of the outer portion of this horny projection. Now, if, as Darier asserts, these horny masses that project, in the advanced stages of the disease, half an inch above the level of the skin, are almost entirely made up of psorosperms, and if these bodies, when situated in the stratum granulo-

sum, contain granules similar to those characteristic of this layer, and, when in the stratum corneum, show the same reaction to staining agents as do the tissue cells—we are forced to the conclusion that they undergo at least a partial keratosis, or, in other words, are subject to much the same changes that affect the tissue cells proper—a phenomenon for which, so far as I am aware, we have no analogy in the history of animal parasites. In reply, it may be urged that the coccidiæ are so closely incorporated in the epithelial cells of the stratum granulosum that the eleidine granules, which have every appearance of filling the psorosperm-like body, are in reality situated in the cell which envelops it; but even if this be granted, the fact that we have, in addition, a hyperkeratosis, can not, it seems to me, be denied. An analogy, too, may be found in the recent able article of Neisser on "*Epithelioma contagiosum*."* This author, while recognizing the molluscum bodies to be made up largely of gregarinæ, another variety of the sporozoa, states emphatically that there occurs at the same time an exaggerated keratosis of the epithelial structures. Leloir and Vidal† also conclude that there is a hyperkeratosis in these lesions, although they express themselves with rather more reserve as to the parasitic nature of the molluscum cells. In any event, with regard to these two cases, it seems to me impossible to escape from the conclusion that there is present and continually active a *hyperkeratosis in the cutaneous lesions*.

These bodies strongly suggest, as Darier has observed, certain peculiar cell elements found in cancer. A number of specimens of flat-celled epithelioma, examined for purposes of comparison, offer appearances very similar to the psorosperm-like cells of these cases. Moreover, I have found in a specimen of verruca vulgaris round cells in the rete Malpighii, considerably larger than those surrounding them, containing a nucleus more or less well defined, of a glistening appearance, and with an apparent retraction of the protoplasm from the periphery, so that nucleus and protoplasm appear as if surrounded by a clear space. In the hypertrophied horny layer above, the outline of these bodies, unstained by the alum carmine, could occasionally be seen. These bodies presented many points of analogy with those found in the two cases, as was readily acknowledged by all to whom I showed these specimens. Are we to regard these also as a species of psorosperms?

Attempts were made to obtain some further light by cultures on agar plates, in water, and in bouillon, but with no result. Inoculation experiments were also made on animals, but these too have been entirely negative up to the present time. Lastly, I have to record my failure to produce a differential or distinctive staining of these bodies.

It can not be denied that many good reasons have been offered by the admirable paper of Darier for considering it not improbable that these bodies may be proved to be coccidiæ. So little, however, is known by zoölogists of this class of parasite, and its organism is so low in the scale (differing as it does so slightly from a tissue cell), that we are justified in demanding strong proof before fully admitting that the peculiar cell-forms in question are to

* "*Vierteljahresschrift für Derm. und Syph.*," 1888, 4. Heft.

† "*Traité descriptif des maladies de la peau*," Paris, 1889.

be placed here. We can not, therefore, accept their parasitic nature as beyond all doubt until some positive proof is offered by culture or inoculation, or at least until some further analogy with the sporozoa can be shown.

Very truly yours, JOHN T. BOWEN.

The following questions naturally suggest themselves in our study of these cases in attempting to form a positive conclusion as to their true nature:

1. Have the bodies in question been found in every case of this rare affection?

As they have occurred in all four instances—the two cases reported in Paris and the two described by myself, which have been observed since attention has been especially called to their presence by Darier—it would be fair to assume that they will be found in all future cases.

2. Do they occur in every affected follicle—that is, in all the lesions of the disease?

This is a question of most important bearing upon their ætiological relations. Of course, a positive answer can not be given to it in such a case as my first one, because it presented myriads of lesions; but, inasmuch as they were found in every one of the many examined and in every phase of their development, as well as in those of the other patients, it may be assumed, perhaps fairly, that they are uniformly present.

3. Are these bodies parasites?

This question must be settled by the histologist and zoölogist. Several distinguished dermatologists at the Paris Congress—men like Unna, for example, who are thoroughly familiar with the minute anatomy of the cutaneous tissues in health and disease—told me that they must so regard them; but their opinions were based upon a mere inspection of the microscopic sections on view. My colleagues in the anatomical and pathological departments of Harvard University, also well acquainted with the minute appearances of human structures, hesitate to pronounce them of extraneous character. Prof. Joseph Leidy, of Philadelphia, than whom no one is more competent to express an opinion upon their nature as a zoölogist, has very kindly examined specimens of the lesions from both my cases. He writes: "I have examined your preparations of the skin and have observed the large, nucleated cell-bodies in the epidermal layers, but feel uncertain as to their true character. They may, perhaps, be of the nature of psorosperms, to which they bear a resemblance, but I am not satisfied that they are such." It seems to me that Dr. Bowen very fairly states the uncertainties which surround the positive settlement of this question. No definite inference upon this point can be drawn, I think, from the action of parasiticides thus far used in the treatment of these cases.

4. Do these bodies cause the tissue changes in the disease in which they are found?

If we look upon them as parasites and not the product of the disease, there is no improbability in regarding them as its cause, in view of the much more serious and complicated modifications of cutaneous tissues which foreign organisms of much less magnitude and simplicity of structure are capable of exciting—the bacilli of leprosy and tuberculosis, for example. On the other hand, we should not forget that animal parasites of relatively high organization—the *demodex folliculorum*—may inhabit the orifices of the sebaceous glands indefinitely without producing any recognizable tissue change.

5. Are these bodies communicable from one person to another? Is the affection contagious?

Our evidence upon these points is wholly of a negative character. The experiments made by Darier to establish new colonies of the bodies upon other animal tissues failed uniformly, as did those of Dr. Bowen in this direction. That they might readily be transferred from an affected follicle to adjoining follicles in the processes of washing the skin, scratching, or by the clothing, may be easily understood; so that, in time, animal parasites without power of motion, like the mycoses, could affect the whole surface, as in my first case. We have no clinical proof of the transference of the disease from one person to another, although two of the four cases under consideration were affected husbands living with their wives. Such negative data are of little value, however, upon the point under consideration. It is well known that tinea versicolor may affect one of a married couple for many years without being communicated to the other.

6. Are these bodies found in other dermatoses?

If it can be shown that they are found in other diseased conditions of the skin in which the characteristic tissue changes are wholly unlike those of the affection under consideration, or that their occurrence in healthy follicles shall be found to be by no means rare, then grave doubts might well arise as to their pathognomonic relation to our cases. It has been above noted that the peculiar bodies found in molluscum epitheliale or contagiosum, as to the nature of which much diversity of opinion has long prevailed, are regarded by Darier and others as coccidiæ also, and that Dr. Wickham claims that similar bodies are found in and are the cause of Paget's disease. The cutaneous lesions in these three affections are certainly wholly unlike in a most significant degree. Dr. Bowen calls attention to the occurrence of cells, strongly resembling the bodies in question, in other diseased conditions of the skin. A too universal discovery of their association with dermal pathology should throw grave suspicion upon them as an ætiological factor in any single dermatosis.

The real nature of these rare instances of disease can not be regarded as definitely settled, in my opinion, or all the conclusions of M. Darier be accepted, until we have obtained more satisfactory information than we now possess upon the questions above raised.

